POST-OPERATIVE PAIN FOLLOWING TREATMENT USING THE GENTLEWAVE SYSTEM: A RANDOMIZED CONTROLLED TRIAL

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DEDICATION

To my wonderful wife Kayka, the backbone and support in my life

To my parents for always pushing me to strive for success

To my mother in-law, for being there when Kayka and I truly needed you.

ABSTRACT

INTRODUCTION: Cleaning and shaping are necessary to allow for the delivery of irrigants and medicaments to the apical third of the canal. Standard treatment irrigation generally uses a conventional needle and some frequency of sonic activation. The GentleWave® system (GWS) (Sonendo, Inc, Laguna Hills, CA) combines irrigant delivery with Multisonic activation. The aim of this randomized clinical trial was to determine if the GWS significantly decreases the incidence and intensity of post-operative pain.

METHODS: Patients used a numerical rating scale (NRS) to record their pain level at the six-hour timepoint before treatment. All participants were randomly divided into two groups and were blind to the treatment they received. The standard (control) group received endodontic treatment with conventional side-vented needle irrigation and ultrasonic activation. The 2nd group received treatment with the GWS. Following treatment, patients used an NRS to record their pain level at six, 24, 72, and 168 hours

RESULTS: 72.2% of standard treatment patients and 83.3% of GWS patients experienced at least one occurrence of post-operative pain. The highest pain intensity level for both treatments occurred at the six-hour post-treatment timepoint. The mean pain intensity for standard treatment was 23.22 (+/- 25.38) and for GWS treatment intensity = 11.56 (+/- 9.94) ($p = 0.0826$). All pain decreased with time after the six-hour post-treatment time point ($p < 0.0000001237$).

CONCLUSION: There was no significant difference in the incidence or intensity of post-operative pain following either treatment group. However, both groups reported a statistically significant decrease in pain with time.

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INTRODUCTION

There are many reasons why a tooth would need root canal treatment. Root canal treatment is indicated once a tooth reaches a level of inflammation or infection where healing can no longer occur. This inflammation or infection can eventually lead to periradicular disease. The goal of root canal treatment is to clean, shape, disinfect, and obturate all canal systems within the tooth in order to prevent periradicular disease from occurring or to eliminate the etiology of existing periradicular disease. As a means of fulfilling these goals, Dr. Schilder in 1974, presented a standard for root canal treatment with his mechanical and biological principles for cleaning and shaping the root canal system (1). This process of cleaning and shaping is completed using hand or rotary files. The purpose of this mechanical cleaning and shaping is to allow for the delivery of irrigants and medicaments to the apical third of the canal (2). Although most of the canal space disinfection occurs during mechanical preparation (3), the irrigant used and the method of irrigant delivery are essential to the complete chemomechanical disinfection of the root canal space.

If the canal system has been properly instrumented, there will be adequate space created for the delivery of irrigants. The use of irrigants not only lubricates and disinfects the canal system but also aids in the removal of contaminants and debris (2). The most commonly used endodontic irrigant is sodium hypochlorite (NaOCl) (4). NaOCl has bacterial killing capabilities and is capable of dissolving necrotic tissue, vital pulp tissue, and the organic components of dentin and biofilms in a fast manner (2). Other than NaOCl, Chlorhexidine (CHX) and Iodine potassium iodide (IKI) are also disinfecting irrigants that are frequently

used. In addition to disinfecting agents, chelating agents are commonly used to remove inorganic material from the canal system to help facilitate smear layer removal (5). Ethylenediaminetetraacetic acid (EDTA) is a chelating agent that removes calcium ions and other inorganic material from dentinal walls within the root canal (6). Additional chelating agents include Citric Acid, MTAD, tetracycline and Maleic Acid (7). Generally, the safest and most common method for the delivery of irrigants is the conventional side-vented needle (8). However, there are additional methods of irrigant delivery that can be used depending on the situation. These methods include the EndoVac® (Kerr™ Corporation, Brea, CA), Quantec-E® (SybronEndo, Orange, CA), RinsEndo (Air Techniques, Mehlville, NY), and the GentleWave® system (GWS) (Sonendo, Inc, Laguna Hills, CA).

Between appointments, or hours to days after the completion of treatment, post-operative discomfort or pain can occur due to acute inflammation (9). The factors most commonly responsible for interappointment or post-operative pain include mechanical preparation and obturation beyond the apex, bacteria not eliminated during primary disinfection, and extrusion of chemical irrigation material beyond the apex (10). In addition to the procedural complications that can lead to post-operative pain, Gotler et al 2012, found that post-operative pain typically occurs at an increased incidence and higher severity in retreatments and vital teeth, as opposed to necrotic teeth (11). In addition, Mattscheck et al 2001, found that patients experiencing pre-treatment pain are more likely to experience post-treatment pain (12).

As mentioned above, irrigant extrusion is a complication that can lead to post-operative pain. With a conventional side-vented needle, the depth of needle penetration and the

pressure placed on the syringe plunger are both under operator control and can be adjusted to avoid irrigant extrusion. The GWS, on the other hand, avoids extrusion by relying on the negative pressure created by the suction within the device (13). Whether or not the GWS extrudes irrigants, has been a question of concern from various clinicians. This possible extrusion could lead to negative results such as necrosis, ecchymosis, or post-operative pain. Only two clinical studies to date have examined the occurrence of post-operative pain following treatment using the GWS. The purpose of this randomized clinical trial was to determine whether treatment using the GWS significantly decreases the incidence and intensity of post-operative pain following root canal treatment.

REVIEW OF THE LITERATURE

Cleaning and Shaping

Successful endodontic therapy is based on the biological and mechanical objectives introduced by Schilder in 1974. These biological objectives include: 1) To confine the procedures within the roots themselves, 2) To not force necrotic debris beyond the foramina, 3) To remove all tissue from the root canal space, and 4) To create sufficient intracanal space for medicaments and irrigants (1). Subsequently, Peters et al 2016, also presented basic objectives in cleaning and shaping which include: 1) Remove infected soft and hard tissue, 2) Give disinfecting irrigants access to the apical canal space, 3) Create space for the delivery of medicaments and obturation, and 4) Retain the integrity of radicular structures (2). Both sets of objectives were established to ensure complete cleaning and disinfection of the root canal space, with mechanical instrumentation removing anywhere from 80-100% of cultivable bacteria (3, 14, 15, 16). In order to prevent occurrence of periradicular disease, or allow the body's immune system to heal existing periradicular disease, a well-executed root canal preparation is a prerequisite for success (17). There are several variations of hand and rotary file systems and techniques that an operator can use to complete the instrumentation of the root canal system.

Irrigant Solution

Irrigation is a critical supplement for mechanical debridement. Irrigation is responsible for flushing pulpal debris and dentinal shavings out of the canal system. In order to eliminate

the cause of infection and apical periodontitis, irrigants must be able to reach the apical third of the canal space. Approximated 27% of teeth have accessory canals and 17% of those accessory canals, known as apical deltas and ramifications, are located in the apical third of the canal (18). These apical deltas can hold necrotic debris and bacteria, which can lead to post-operative pain, inflammation, or recurrent apical disease. An optimal irrigation protocol is based on the combined use of 2 or several irrigating solutions to predictably and safely irrigate the canal space (5). Sodium hypochlorite is an alkaline fluid with a pH of approximately 11-12. It hydrolyzes proteins and causes hemolysis of red blood cells, which leads to the dissolution of both vital and necrotic tissue. Upon contacting organic debris, hypochlorous acid forms which disrupts bacterial metabolism by oxidizing the sulfhydryl group of bacterial enzymes. NaOCl has broad antibacterial coverage and also effective against spores and viruses. Its efficacy depends on the concentration, temperature, and exposure to sunlight and vibration. Disinfecting concentrations generally range from 0.5% to 5.25%. 5.25% NaOCl has a better antimicrobial effect and is more effective at dissolving necrotic tissue than lower concentrations (19). Although not as effective, CHX is another disinfecting irrigant that has prolonged antibacterial efficacy and can be used safely in cases where perforation or extrusion is likely. It has a pH range of 5.5 - 7, and is used at a concentration of 2% for root canal therapy. In addition to a disinfecting irrigant, a chelating agent is necessary to remove the smear layer created by instrumentation. Removal of the smear layer not only allows for complete disinfection of the root canal system, but also for improved trans-dentinal diffusion of calcium ions when medicating the tooth between appointments, and deeper sealer penetration when obturating the tooth. As previously

noted, EDTA is a commonly used chelating agent. It has a pH range of 7.5 - 9 and is most commonly used at a concentration of 17%. Citric acid is also a chelating agent, which is used in concentrations ranging from 1% to 50%. Finally, MTAD is a chelating agent that is a combination of doxycycline, citric acid, and a detergent. It is not commonly used because of its tendency to cause tetracycline resistance in bacteria.

Irrigant Delivery

Aside from the preferred irrigants and their concentration, the delivery system selected is also important. Irrigation needle tip design determines the flow pattern, velocity, pressure, and overall safety and effectiveness of irrigants (5). Although conventional side-vented needles are perceived to be advantageous for the prevention of apical extrusion (8), Shen et al 2010, found that regardless of the needle design, all needles placed 3 mm from the apex will cause irrigant to reach the apical terminus (20). This distance should be continuously monitored, especially in cases where extrusion is likely, because many irrigants are cytotoxic and can cause necrosis and extreme pain when extruded beyond the apex (21). Supplementary systems for irrigant delivery include the Quantec-E irrigation system, which attaches to an endodontic handpiece for continuous irrigant delivery during rotary preparation. The Rinsendo is an automated irrigation system that uses compressed air to deliver irrigants under positive hydrodynamic pressure; and the EndoVac uses negative pressure to pull irrigant down the canal in order to avoid extrusion. The GWS, to be discussed later, is a novel irrigant delivery system that uses degassed irrigant solutions and broad-spectrum acoustic energy to remove tissue and debris (22).

Irrigant Activation

In conjunction with the types of chemical irrigants chosen, activation of the irrigant by hand, subsonic, sonic, or ultrasonic activation can enhance the cleaning of the canal system. An example of a subsonic instrument is the EndoActivator® (Dentsply Sirona, Inc, Charlotte, NC) which activates irrigants at frequencies in the range of 2000-10,000 cycles per minute (cpm, 33.3-166.7 Hz) (23). Sonic instruments operate between 1-8 kHz, these instruments force compressed air through a driver to create oscillations. Finally, ultrasonic instruments operate between 25-40 kHz via one of two ways. They are either magnetostrictive, where an electric current passes through metal plates producing a magnetic field, which causes vibrations; or piezoelectric, where an electric current passes through a crystal causing the crystal to change shape thus creating mechanical oscillations. The use of ultrasonic energy not only creates acoustic streaming that aids debridement (24, 25), it also pushes the irrigant deeper into dentin tubules, lateral canals and isthmuses, which promotes better cleaning of the canal system (26, 27, 28). Sonically activating irrigants also increases the antibacterial efficacy to seven times greater than instrumentation alone (29). Thirty seconds of activation produces significantly cleaner canals than filing alone in the apical third of the canal system (30, 31), and the activation of irrigants also allows for a better seal of root filling materials (32). All of these activation techniques have the potential to cause irrigant and debris extrusion (33), however, if placed within 1mm of the working length, each technique should be safe not to cause apical extrusion (34).

GentleWave System (GWS)

The GWS is an FDA cleared root canal irrigation device that creates vortexes of internally degassed 3% NaOCl, sterile water, and 8% EDTA. These irrigants travel through the root canal system at separate timed intervals. The vortexes, along with broad-spectrum multisonic acoustic energy, cleans debris from canal walls and disinfects the entire root canal system (35). The broad-spectrum of acoustic energy creates hydrodynamic cavitation and thousands of microbubbles that create powerful shear forces, similar to ultrasonic activation (22). Cleaning and shaping when using the GWS requires all canals to be instrumented to a minimum master apical file size of 15 or 20 before the GWS can be used for irrigation (36). The GWS utilizes different pressure settings to treat anteriors/premolars, and molars. The system also relies on a negative pressure to prevent the extrusion of irrigant into periapical tissues. Use of the GWS is contraindicated in teeth with immature apices, teeth with insufficient coronal structure, teeth with coronal caries or deficient crown margins, and teeth with root apices extending into the maxillary sinus.

Post-operative Pain

A flare-up is an acute exacerbation of periradicular pathosis, which can include severe pain or swelling (9). This can occur between appointments after root canal treatment has been initiated or after a tooth has been obturated and treatment has been completed. Pre-treatment pain, retreatment of teeth, and molar teeth are all positively correlated with the occurrence of post-operative pain (37, 38). Mattscheck et al 2001, found that those patients with a pretreatment pain of greater than 20 on a visual analog scale (VAS) have

significantly more post-treatment pain up to 24 hours following treatment (12). A meta-analysis by Tsesis et al 2008, found the average rate of flare-ups to be 8.4% with no conclusions able to be drawn from influencing factors (39). Studies by Harrison in 1983, found the incidence of moderate to severe inter-appointment and post-operative pain to be 15.7%-47.6% with a greater likelihood of pain occurring within 24 hours; and a study looking at healing following treatment with the GWS found mild post-operative pain to occur in 15.6% of patients for up to 2 days following treatment (40, 41, 42). When considering whether single appointment versus multiple appointments cause more flare-ups or post-operative pain, Trope in 1991, found in teeth with apical periodontitis, only 1.4% of patients experienced a flare-up with a single visit (43). Whereas studies by Ng et al 2004 and Sathorn et al 2008, found that there was no significant difference between single and multiple visit treatments, with an incidence of up to 58% experiencing post-operative pain (44, 45).

Pain Survey

When assessing a patient's pain, the patient's self-report is the most accurate and reliable evidence of the existence of pain and its intensity (46). There are several approaches to pain self-measurement, which range from numeric and verbal rating scales to psychological scales. The main role of a pain scale is to measure the severity of pain and if it changes over time (47). Although the VAS is one of the most widely used tools to survey the severity and relief of pain, the Numeric Rating Scale (NRS) is regarded as one of the best single-item methods available to estimate the intensity of pain (48, 49).

Hjermstad et al 2011, found that the NRS is the preferred method of pain analysis by patients because it simplified how to describe their pain (50, 51). Similar to a VAS, with the NRS, patients are responsible for selecting the number that best represents their pain or discomfort on a numbered scale, which serves as the continuum between "no pain" and "the worst pain ever felt" (52). However, there is no shrinking or enlargement error created with reproducing the NRS as there is with the VAS. Data obtained via a NRS are easily interpreted, documented, and meet regulatory requirements for pain assessment (53).

Pain Control

Following any endodontic procedure, there is always a chance that pain or discomfort can occur. Should any post-operative pain occur, a protocol is necessary to successfully manage the discomfort. Non-Steroidal Anti-inflammatory Drugs (NSAIDs) are the drug of choice to alleviate or minimize endodontic pain (54) and most studies support the use of NSAIDs post operatively, as long as there is no contraindication to taking them. At standard doses, ibuprofen is far superior to acetaminophen at producing a worthwhile feeling of pain relief (55). 600 mg ibuprofen has been shown to reduce the intensity of endodontic pain by 76% and the combination of 600 mg ibuprofen plus 1000 mg acetaminophen reduces the intensity of endodontic pain by 96% (56). When compared to opioids of various potency, NSAIDs have been shown to lower baseline pain and have less toxicity in patients taking both consistently for severe, persistent pain (57). Antibiotic use is generally not recommended for pain relief unless indicated, as this has been shown to

increase bacterial resistance and interfere with the growth of normal gut flora (58).

SPECIFIC AIMS

1. To determine whether irrigation with the GentleWave system will significantly decrease the incidence of post-operative pain following endodontic treatment.
2. To determine the intensity of post-operative pain, should it occur, based on a numerical rating scale for pain assessment.

NULL HYPOTHESIS

There is no difference in the incidence or intensity of post-operative pain following instrumentation and irrigation using a standard endodontic treatment protocol versus instrumentation and irrigation using the GentleWave system for cleaning and disinfection of the root canal system.

MATERIALS AND METHODS

Ethics

This study was approved by the Institutional Review Board (IRB) at the University of Minnesota, Twin Cities (STUDY00003030). This study was also registered in the ClinicalTrials.gov database (NCT03635515) and registered with the University of Minnesota OnCore clinical trial management system (DENT-2018-26373). All patients signed informed consent and HIPAA authorization forms after agreeing to participate in the study.

Research Design

This study was a single blind, randomized, controlled clinical trial comparing the incidence and intensity of post-operative pain following root canal treatment. Following a standard endodontic cleaning and shaping protocol, the independent variables were irrigation using a conventional side-vented needle for irrigant delivery combined with ultrasonic activation and irrigation using the GWS. Three 2nd year residents in the Graduate Endodontics department at the University of Minnesota School of Dentistry performed all treatments. In order to calculate required sample size necessary to achieve a power of 80%, several studies were examined. These studies were used to determine the anticipated incidence of post-operative pain following a standard endodontic treatment protocol and treatment with the GWS. Using the Pak et al 2011 and Sathorn et al 2008 systematic reviews, and the Sigurdsson et al 2016 and 2018 studies on the GWS, the anticipated incidence of post-

operative pain was determined to be 60% and 15%, for the standard treatment and the GWS treatment, respectively (59, 45, 36, 42). Thus a sample size of 34 patients (17 per group) was deemed necessary to achieve a power of 80%. The IRB restricted recruitment size to 50 patients (25 per group), allowing for possible loss to follow-up during the study duration. The study's target population included patients of the Graduate Endodontics clinic requiring root canal treatment. Inclusion criteria were: (i) patients who were 18 years of age or older, with a molar or premolar requiring root canal therapy, (ii) teeth with fully formed apices. Exclusion criteria were: (i) patients under the age of 18 or those patients incapable of giving informed self-consent, (ii) teeth with immature apices, (iii) teeth with apices in the maxillary sinus or those teeth where the apical lesion had eroded the bone of the maxillary sinus floor, (iv) teeth with internal or external resorption, and (v) teeth with carious lesions or deficient crowns that cannot be repaired before accessing the pulp chamber. Prior to treatment, a diagnostic exam and testing were performed that included a cold test, percussion and palpation testing, mobility and periodontal probing, and a radiographic exam. Patients were then asked to record the level of pain they experienced six hours prior to treatment. If the treatment required 2 appointments, the 6-hour pre-treatment pain assessment was taken prior to the second appointment. These measurements were made using a 0-100 NRS-41 pain assessment (Figure 2, Appendix II). The '0' mark represented 'no pain' and the '100' mark represented 'the worst pain imaginable'. There were 39 additional numeric markings between the '0' and '100' that patients could choose. Patients were also instructed to write in their pain rating if it was not sufficiently represented on the scale. Along with the numeric scale, the surveys included Wong-Baker

FACES corresponding with six separate pain ratings, as well as verbal markers indicating low, mild, moderate, high, and very high pain. For the purposes of this study, scores 0-19 represented low pain, 20-39 was mild pain, 40-59 was moderate pain, 60-79 was high pain, and 80-100 was very high or severe pain. List randomization software was used to generate a list for random patient assignment as they were recruited.

Patients were divided into one of two treatment groups. For both groups, local anesthetic was delivered via infiltration for maxillary teeth using a 30 gauge needle and via inferior alveolar nerve block or gow gates for mandibular teeth using a 27 gauge needle. Prior to accessing the pulp chamber, all caries, defective restorations, and deficient crowns were removed. A pre-endo build-up was placed if necessary, to maintain isolation. Straight-line access to the pulp orifices was then achieved. A size (#) 8 or 10 K-file and the Root ZX II electric apex locator (J. Morita Corp, Osaka, Japan) were used to determine the working length, which was then verified with a periapical radiograph.

For the control (standard endodontic treatment) group, following working length determination, all canals were instrumented using hand and rotary files to at least a minimum size and taper of 25/04 to within ½ to 1 mm short of the apical terminus. The treating clinician determined the appropriate final apical canal size based on tooth morphology. Canals were prepared in a crown down fashion to avoid debris and irrigant extrusion. Between each file, 5.25% NaOCl was used to disinfect the canals and flush debris. Recapitulation with a #8 or #10 K-file was performed to maintain patency. Following instrumentation, NaOCl was ultrasonically activated for 30 seconds in each canal using the Spartan Wave™ Piezo (Obtura Spartan Endodontics, Algonquin, IL)

ultrasonic unit. Each tooth was then flushed with 3 ml of 17% EDTA for 1 minute followed by a rinse of 5.25% NaOCl. A total of at least 10 ml of NaOCl was used for each procedure. A final rinse of 1 ml of 95% ethanol was used prior to the obturation of all procedures except for those sealed with bioceramic sealers. Canals were then dried and filled with gutta-percha and a sealer of the clinician's choice.

For the GWS group, following working length determination, all canals were instrumented to at least a minimum size and taper of 20/04 or 06 to within ½ to 1 mm short of the apical terminus. The treating clinician determined the appropriate final canal size based on tooth morphology. Canals were prepared in a crown down fashion to avoid debris and irrigant extrusion. Between each file, 5.25% NaOCl was used to disinfect the canals and flush debris. Recapitulation with a size 8 or 10 K-file was performed to maintain patency. Following instrumentation of the canals, the GWS occlusal platform matrix was placed onto the tooth into the access cavity to verify the correct access opening size. Kool-dam heatless liquid dam (Pulpdent, Watertown, MA) was then placed on the GWS occlusal matrix to build an occlusal platform to support the GWS handpiece and seal the access opening. The tooth was re-accessed to the same size as the original access opening. For molars, the GWS depth gauges were used to determine the proper sealing cap for the GWS handpiece. Following calibration and cycle selection, the GWS handpiece was then positioned on the tooth for the entirety of the treatment cycle, which varied in length of time depending on the tooth type. The GWS delivered 50 +/- 10 ml of irrigant fluid per minute for molar treatments and 35 +/- 10 ml for premolars. Canals were then dried and filled with gutta-percha and a sealer of the clinician's choice.

Once obturation and temporary or permanent restoration were completed for patients in both groups, patients were given a similar 0-100 scale NRS-41 pain assessment to take home and were asked to record their pain levels at 6, 24, 72, and 168 hours post-treatment (Figure 3, Appendix II). In order to control any pain that may have been unbearable, patients were instructed to use a rescue medication and to record the drug doses. This rescue medication was the ibuprofen and acetaminophen regimen introduced by Menhinick et al in 2004.

Statistical Method

A two-sample t-test was run with a significance level of 0.05 for pain measurements recorded at six, 24, 72, and 168 hours. A linear mixed effects model was used to compare the groups across time.

RESULTS

A total of 44 patients were recruited for the study. The patient's ages ranged from 24 to 81 years of age. Twenty-five patients were male and 19 were female. 36 out of 44 patients (18 in each group) returned their NRS-41 pain assessments for a recall rate of 81.8%. Four patients in both the standard treatment group and the GWS group were lost to follow-up. One case in the GWS group was lost to follow-up due to a separated file being pushed into the apical periodontal tissue during the GWS treatment, this subsequently changed the prognosis of the tooth and treatment plan. One tooth in the standard treatment group was lost to follow-up due to a procedural error occurring during post placement by the restoring doctor, which condemned the tooth. This occurred the same day following the root canal treatment. In the GWS group, 77.8% were molars and 22.2% were premolars. In the standard treatment group, 66.7% were molars and 33.3% were premolars. Most teeth were instrumented with either Vortex Blue files (VB, Dentsply Sirona, Inc, Charlotte, NC) or EndoSequence® Scout files (Brassler USA, Inc, Savannah, GA) and a majority of cases were instrumented to a master apical prep size and taper of 30/04 with the lowest being 20/04 and the highest being 40/04. AH Plus (Dentsply Maillefer, Ballaigues, Switzerland) and EndoSequence® BC sealers (Standard & HiFlow, Brassler USA, Inc, Savannah, GA) were used during the obturation of most cases. Two cases were completed with Kerr EWT sealer (Kerr™ Corporation, Brea, CA) and one case was completed with Roth 801 sealer (Roth Pharmacy, Chicago, IL). The obturation technique of choice was either a modified

continuous-wave (MCW) or a single cone (SC) technique. There was no significant difference found with any of these variables.

As shown in Table 1, 72.2% (13/18) of standard treatment patients reported at least one incidence of post-operative sensitivity with 76.9% of those patients having greater sensitivity after treatment than before. 55.6% (10/18) of patients had some level of pre-treatment pain. 90% (9/10) of pre-treatment pain patients experienced post-operative pain. Three out of nine had pain up to at least 72 hours following treatment, and the other six still had pain of varying intensities at the 1-week timepoint. Of the eight patients who had no pre-treatment pain, half experienced no post-operative pain and the other half only experienced low or mild pain (0-39). Three experienced pain up to 24 hours following treatment and one experienced pain up to 3 days following treatment.

STANDARD TREATMENT PATIENTS

	Cases	Post-Tx Pain	Pre-Tx Pain	6 hrs	24 hrs	72 hrs	168 hrs
Total	18	13 (72.2%)	10 (55.6%)	13 (72.2%)	11 (61.1%)	10 (55.6%)	6 (33.3%)
Low (1-19)			6	5 (27.8%)	2 (11.1%)	6 (33.3%)	4 (22.2%)
Mild (20-39)			2	2 (11.1%)	6 (33.3%)	2 (11.1%)	2 (11.1%)
Moderate (40-59)			0	4 (22.2%)	2 (11.1%)	1 (5.6%)	0
High (60-79)			1	2 (11.1%)	0	1 (5.6%)	0
Severe (80-100)			1	0	1 (5.6%)	0	0

Table 1: Pain Incidence/intensity reported by standard treatment patients

Table 2 shows that 83.3% (15/18) of GWS patients experienced at least one incidence of post-operative pain. Three patients had pre-treatment pain and 12 had no pain prior to treatment. Of the 12 patients who were pain-free prior to treatment, four patients only had pain six hours after treatment, two patients had pain up to 24 hours following treatment, two patients had pain up to 72 hours following treatment, and three patients had pain up to 1 week following treatment. Finally, one patient had no pain following treatment up until the 72-hour timepoint, which subsided before the 1-week timepoint. Of the three patients who had pretreatment pain, one patient only had pain up to 6 hours following treatment and the other two had no pain after 72 hours.

GENTLEWAVE PATIENTS

	Cases	Post-Tx Pain	(-) 6 hrs	6 hrs	24 hrs	72 hrs	168 hrs
Total	18	15 (83.3%)	3 (16.7%)	13 (72.2%)	9 (50%)	8 (44.4%)	3 (16.7%)
Low (1-19)			1	8 (44.4%)	7 (38.9%)	7 (38.9%)	1 (5.6%)
Mild (20-39)			2	5 (27.8%)	1 (5.6%)	1 (5.6%)	2 (11.1%)
Moderate (40-59)			0	0	1 (5.6%)	0	0
High (60-79)			0	0	0	0	0
Severe (80-100)			0	0	0	0	0

Table 2: Pain intensity reported by GentleWave patients

When considering post-operative pain intensity, the was no statistically significant difference found following either treatment. Although the GWS created pain that was clinically less severe than that of the standard treatment, there was a greater number of GWS patients who started their only or final appointment with no pain. The highest pain rating following the GWS treatment was '40' reported from one patient at the 24-hour time-point, which is moderate pain. Six standard treatment patients reported either moderate, high, or severe pain during at least one of the designated timepoints up to 72 hours. The highest pain rating following the standard treatment was '80', which is severe pain. All pain reported at the 1-week timepoint was either low or mild pain. There was a statistically significant decrease in pain as time progressed from treatment in both treatment arms ($p < .0000001237$).

	GentleWave	Standard	All	p-value
n	18	18	36	
pain.006hrs.pre	3.33 (±8.40)	14.00 (±27.56)	8.67 (±20.79)	0.1318
pain.006hrs.post	11.56 (±9.94)	23.22 (±25.38)	17.39 (±19.89)	0.0829
pain.024hrs.post	7.78 (±10.88)	19.33 (±21.46)	13.56 (±17.76)	0.0522
pain.072hrs.post	5.00 (±7.28)	13.11 (±18.56)	9.06 (±14.49)	0.0982
pain.168hrs.post	2.78 (±7.32)	5.22 (±10.46)	4.00 (±8.98)	0.4229

Table 3: Mean (+/- SD) pain rating for each of the 5 measured timepoints and the p-value of the simple t-test comparing the means of two groups

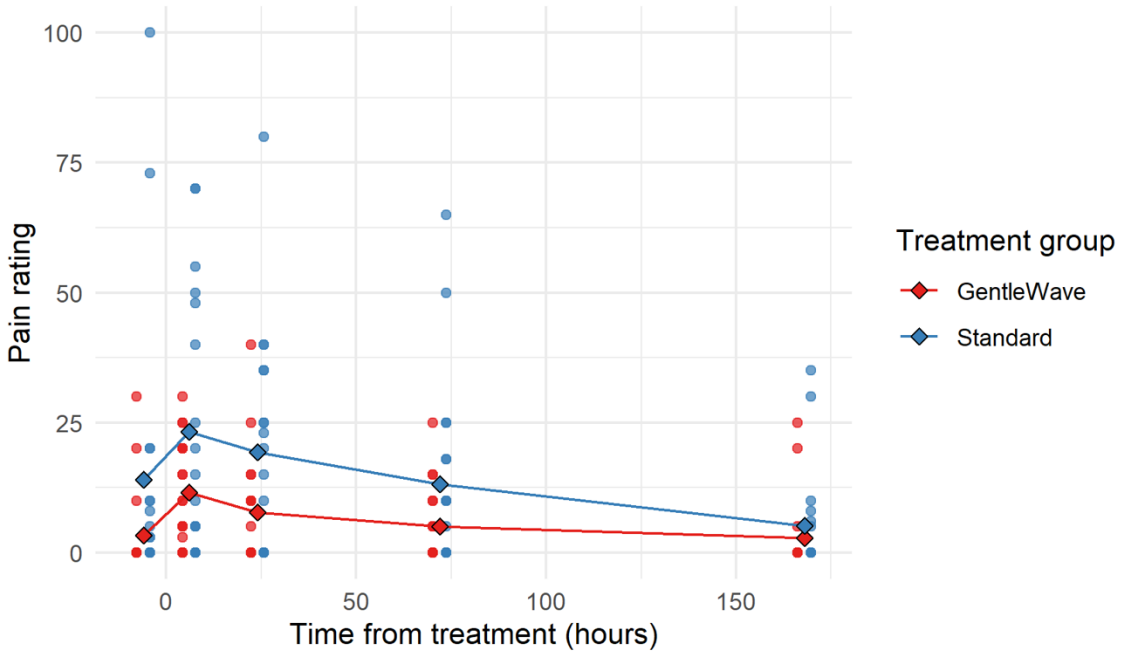

Figure 1: Pain intensity before and after treatment

For patients requiring rescue pain medication, only four patients reported the use of post-operative analgesics to control pain. In the standard treatment group, one patient reported taking 600 mg ibuprofen with 1000 mg acetaminophen every six hours for two days following treatment. In the GWS group, one patient reported taking one dose of 600 mg ibuprofen in the 24 hours following treatment completion. One patient took 600 mg ibuprofen every six hours for 24 hours following treatment. The last patient took one dose of 600 mg ibuprofen immediately following treatment and a second dose six hours after that.

DISCUSSION

Pain has a complex nature and is often considered the fifth vital sign. According to the International Association for the Study of Pain, it is an unpleasant sensory and emotional experience associated with actual or potential tissue damage (46). This study attempted to determine whether there was a significant difference in the incidence and intensity of post-operative pain following treatment with the GWS versus a standard endodontic treatment. The results show there is no statistically significant difference in the incidence or intensity of post-operative pain between the two treatment groups. Out of the 36 patients who returned their pain surveys, 28 reported at least one instance of discomfort following their root canal procedure, for an overall incidence of 77.8%. Thirteen out of 18 of those patients received the standard treatment and 15 out of 18 of those patients received the GWS treatment. Previous studies have found that following root canal treatment using the GWS, patients experience very little post-operative pain, with Sigurdsson et al 2018, finding that only 15.6% of patients experienced 'mild' post-operative discomfort up to 2 days following treatment (42). This was similar to the results found by Harrison et al 1983 when looking at interappointment and post-operative pain following standard root canal treatment (40, 41). There is no way to know the exact cause of post-operative pain. However, there are several factors that could cause a patient to experience this discomfort, which includes local anesthetic choice and technique, pre- or post-treatment analgesia, irrigant extrusion, over-instrumentation, extended periods of mouth opening, or even referred pain from a source that was not addressed with the root canal treatment.

Within this study, there was no difference between the incidence of pain with differing age, tooth type, number of appointments, rotary file system, master apical prep size, type of sealer used, or obturation technique. The larger a canal system is prepared, or the greater number of files used, the greater the chance for procedural errors to occur such as over-instrumentation or irrigant extrusion. The protocol for instrumentation prior to using the GWS is to keep the master apical diameter as small as possible, which is either to 0.15 mm or 0.2 mm, with variable tapers moving coronally (35, 36, 42). However, in the GentleWave arm of this study, there were eight teeth prepared to a final apical diameter of 0.2 mm or 0.25 mm, and six of those patients reported at least one instance of post-operative discomfort. No procedural errors or NaOCl accidents occurred during either arm of treatment. Also, care was taken not to administer any long-acting analgesics or local anesthetic at the end of a procedure which could have confounded the results.

Understanding the reporting habits of patients is another factor to consider when surveying the occurrence of pain following root canal treatment. Normal post-operative instructions typically inform patients of the general discomfort that is expected to be experienced following treatment. This could affect a patient's response to pain and influence whether or not pain is reported. Also if the post-operative pain experienced is of a lesser intensity than what was experienced beforehand, patients may feel inclined to not report that pain either. However, separate studies by Eriksson et al 2014 and Talib et al 2018, both found that patients see a benefit in questionnaires regarding their symptoms if there is a genuine interest displayed by the healthcare professional to use the information gathered to improve treatment practices (51, 60). This factor, or perhaps the instruction to pay more attention to

their state of pain may have resulted in a higher report of pain instances than what has been seen in previous post-operative pain studies (59). Although appraising a patient's pain at a moment in time can be reliable, assessing a patient's history of prior pain or understanding their 'usual' pain may help elicit a better insight into what degree a treatment or injury has affected their overall pain experience. This can also give insight into whether the post-treatment pain experienced is of the same nature as their pre-treatment pain or if it differs in any capacity.

Furthermore, the results of this study show there is a no statistically significant difference in the intensity of post-operative pain when comparing a standard endodontic treatment with treatment using the GWS. Overall, results show that there was clinically less severe pain following treatment using the GWS, and this statistic trended towards significance, which may have been proven with a greater sample size. The standard assessment for pain generally only seeks to know the intensity of the pain, either on a numeric or measured scale. However, there are several factors that can define the effect that pain has on individuals. Pain experience, severity, and duration all add to the definition of what pain is. Pain experience involves the intensity and affect of pain. Pain intensity is the degree to which a patient is in pain, and pain affect is the emotional and psychological disturbance caused by the pain. Pain intensity is easy for most patients to declare and thus is easy to measure by several different methods (61). Pain affect, on the other hand, is much more complicated and difficult to measure because of the social, professional, and historical aspects of pain perception and prior injury. Again, a clinician's post-treatment instructions, informing the patient of the discomfort typically experienced following treatment, could

affect the patient's response to their pain and influence whether or not they choose to report that pain. Pain severity not only involves intensity as well, but also includes the 'degree of disability' or what limitations on daily activities the pain is causing. Although intensity is a characteristic included in both pain experience and severity, it only represents a fraction of the effect that pain has on a patient.

When evaluating pain intensity, determining the survey cut-off points of pain descriptors can be important for interpreting and analyzing data. Sigurdsson et al 2018, used a 10 cm VAS and selected the cut-off points of 6 cm and 8 cm as the upper limits of mild and moderate pain, respectively (42). However, other studies have found that lower cut-off points for mild and moderate pain are better for more accurately categorizing pain intensity. Boonstra et al 2014, found the cut-off points of 3.4 cm and 7.4 cm, on a 10 cm VAS, to be optimal for categorizing mild and moderate pain (62), and Aun et al 1986, found the cut-off points of 4.4 cm and 7.4 cm to be most accurate (63). The 0-100 scale NRS-41 pain assessment used in this study had verbal descriptors superimposed with the numerical ratings, and those cut-off points for mild and moderate pain were 39 and 79, respectively. This corresponded with Hirschfield and Zernikov 2013, who found 4 & 8 on a 0-10 scale NRS to be optimal cut-off points for mild and moderate pain (64). Our pain assessment more accurately subcategorizes numerical pain scores with not only verbal descriptors but also a Wong-Baker FACES pain rating scale to further help patients determine their pain intensity at each timepoint. Farrar et al 2001, found that a 20% change on a NRS, or 20 on a 0-100 scale, between any two timepoints of an assessment is clinically significant (65). This study found that 33.3% (5/15) of both standard treatment and GWS patients

experienced a clinically significant increase in pain between pre- and post-treatment. While a lower number of control group patients reported post-operative discomfort following treatment, the pain scores were on average 7 points higher than the GWS group. This could have been due to the GWS's mechanism of action, or because a greater number of GWS patients started their only or final treatment appointment with no pre-treatment pain. The overall average of pain for both treatment groups was low to mild in nature and most pain states peaked at 6 – 24 hours following treatment.

Although the sample size collected was enough to generate significant power statistically, a greater number of participants could have possibly elicited some statistically significant data differentiating the two treatment modalities. The IRB restricted recruitment size to 50 patients, which could have been due to the novel nature of the GentleWave system and the lack of previous literature surveying post-operative pain with the system. Also the GWS's mechanism of action is nothing like any other method of irrigant delivery currently available. The device delivers between 275 and 350 ml of irrigant solution per 7-8 minute procedure. Conversely, Conventional needle irrigation under direct operator control is intermittently delivering a considerably smaller amount of irrigant over the entire treatment period. Although standard irrigation delivers a lower volume of solution, the irrigant concentration is typically higher which is more effective at dissolving vital and necrotic tissue (19). Additionally, 10 ml of intraoperative NaOCl is sufficient to remove superficial debris and the smear layer. Another limitation was the amount of GWS patients that had multiple appointments. With most of the pain eliminated between appointments, this caused a majority of two-appointment patients to have a pre-treatment pain rating of zero.

Although it was beneficial to see that a significant number of patients without pre-treatment pain experienced some level of discomfort following treatment, more single-appointment treatments may have shown a statistically significant decrease in the pain level between pre- and post-treatment with the GWS. Also, the greater number of GWS patients starting with no pre-treatment pain may have elicited the greater number of lower intensity post-treatment pain ratings.

Future studies should focus on recruiting more participants, making all treatments single-visit, or narrowing the inclusion criteria to include only certain pulpal or apical diagnoses and/or pretreatment pain states (i.e. symptomatic vs asymptomatic apical periodontitis, or irreversible pulpitis vs necrotic pulp). Standardizing more variables can eliminate those factors that can have a greater effect on results.

CONCLUSION

Within the limitations of this study, it can be concluded that:

1) Following treatment using the GentleWave system, there was no statistically significant difference in the incidence of post-operative pain versus a standard endodontic treatment using a conventional side-vented needle and ultrasonic activation.
2) There was no statistically significant difference in the intensity of post-operative pain following treatment with a standard endodontic treatment compared to treatment using the GentleWave system.
3) There was a statistically significant decrease in pain intensity as time progressed following both the standard treatment and treatment using the GentleWave system.

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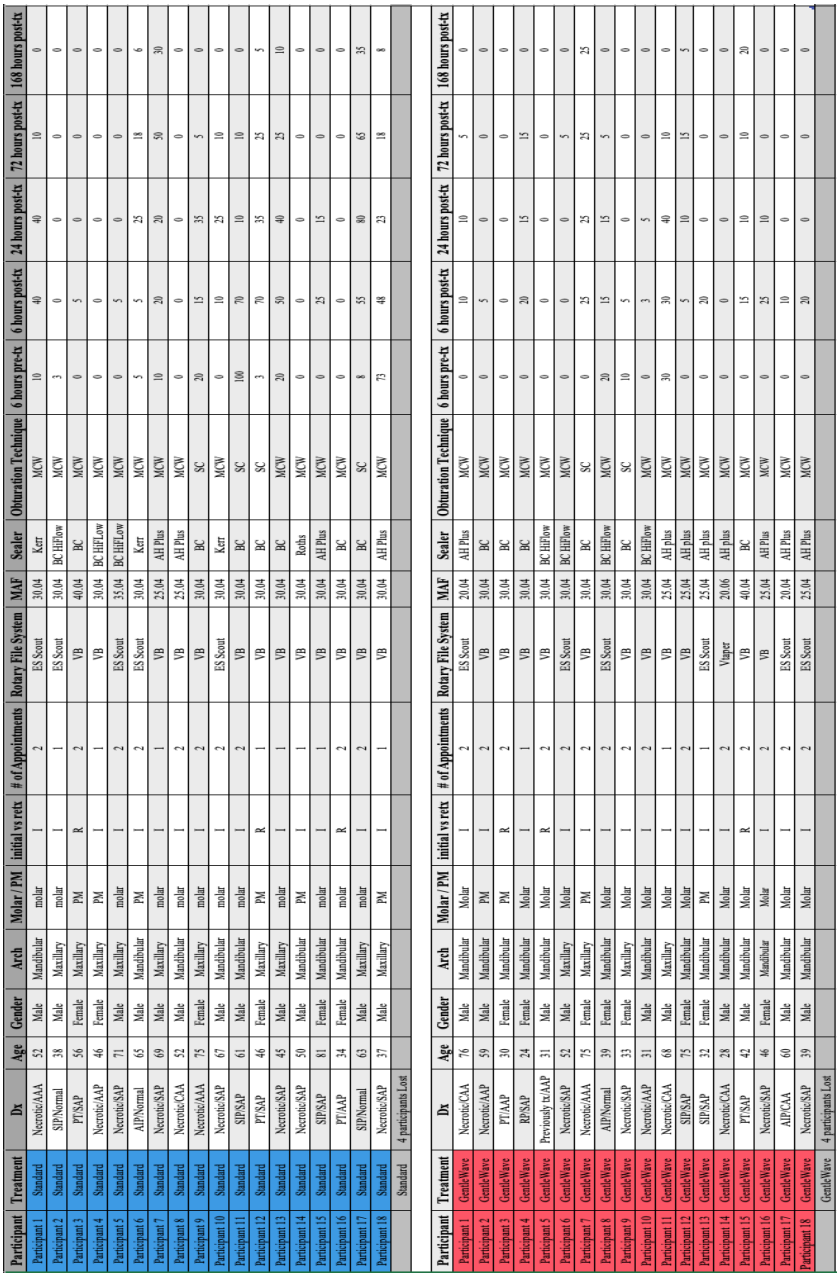
Appendix I

Table 4: Complete Data Collection



Participant	Treatment	Dx	Age	Gender	Arch	Molar / PM	initial vs retx	# of Appointments	Rotary File System	MAF	Sealer	Obturation Technique	6 hours pre-tx	6 hours post-tx	24 hours post-tx	72 hours post-tx	168 hours post-tx
Participant 1	Standard	Necrotic/AAA	52	Male	Mandibular	molar	I	2	ES Scout	30.04	Kerr	MCW	10	40	40	10	0
Participant 2	Standard	SIP/Normal	38	Male	Maxillary	molar	I	1	ES Scout	30.04	BC HiFlow	MCW	3	0	0	0	0
Participant 3	Standard	PT/SAP	56	Female	Maxillary	PM	R	2	VB	40.04	BC	MCW	0	5	0	0	0
Participant 4	Standard	Necrotic/AAP	46	Female	Maxillary	PM	I	1	VB	30.04	BC HiFLow	MCW	0	0	0	0	0
Participant 5	Standard	Necrotic/SAP	71	Male	Maxillary	molar	I	2	ES Scout	35.04	BC HiFLow	MCW	0	5	0	0	0
Participant 6	Standard	AIP/Normal	65	Male	Mandibular	PM	I	2	ES Scout	30.04	Kerr	MCW	5	5	25	18	6
Participant 7	Standard	Necrotic/SAP	69	Male	Maxillary	molar	I	1	VB	25.04	All Plus	MCW	10	20	20	50	30
Participant 8	Standard	Necrotic/CAA	52	Male	Mandibular	molar	I	2	VB	25.04	All Plus	MCW	0	0	0	0	0
Participant 9	Standard	Necrotic/AAA	75	Female	Maxillary	molar	I	2	VB	30.04	BC	SC	20	15	35	5	0
Participant 10	Standard	Necrotic/SAP	67	Male	Mandibular	molar	I	2	ES Scout	30.04	Kerr	MCW	0	10	25	10	0
Participant 11	Standard	SIP/SAP	61	Male	Mandibular	molar	I	2	VB	30.04	BC	SC	100	70	10	10	0
Participant 12	Standard	PT/SAP	46	Female	Maxillary	PM	R	1	VB	30.04	BC	SC	3	70	35	25	5
Participant 13	Standard	Necrotic/SAP	45	Male	Maxillary	molar	I	1	VB	30.04	BC	MCW	20	50	40	25	10
Participant 14	Standard	Necrotic/SAP	50	Male	Mandibular	PM	I	1	VB	30.04	Roths	MCW	0	0	0	0	0
Participant 15	Standard	SIP/SAP	81	Female	Mandibular	molar	I	1	VB	30.04	All Plus	MCW	0	25	15	0	0
Participant 16	Standard	PT/AAP	34	Female	Mandibular	molar	R	2	VB	30.04	BC	MCW	0	0	0	0	0
Participant 17	Standard	SIP/Normal	63	Male	Maxillary	molar	I	2	VB	30.04	BC	SC	8	35	80	65	35
Participant 18	Standard	Necrotic/SAP	37	Male	Maxillary	PM	I	1	VB	30.04	All Plus	MCW	73	48	23	18	8
	Standard	4 participants Lost															

Participant	Treatment	Dx	Age	Gender	Arch	Molar / PM	initial vs retx	# of Appointments	Rotary File System	MAF	Sealer	Obturation Technique	6 hours pre-tx	6 hours post-tx	24 hours post-tx	72 hours post-tx	168 hours post-tx
Participant 1	GentleWave	Necrotic/CAA	76	Male	Mandibular	Molar	I	2	ES Scout	20.04	All Plus	MCW	0	10	10	5	0
Participant 2	GentleWave	Necrotic/AAP	59	Male	Mandibular	PM	I	2	VB	30.04	BC	MCW	0	5	0	0	0
Participant 3	GentleWave	PT/AAP	30	Female	Mandibular	PM	R	2	VB	30.04	BC	MCW	0	0	0	0	0
Participant 4	GentleWave	RP/SAP	24	Female	Mandibular	Molar	I	1	VB	30.04	BC	MCW	0	20	15	15	0
Participant 5	GentleWave	Previously tx/AAP	31	Male	Mandibular	Molar	R	2	VB	30.04	BC HiFlow	MCW	0	0	0	0	0
Participant 6	GentleWave	Necrotic/SAP	52	Male	Maxillary	Molar	I	2	ES Scout	30.04	BC HiFlow	MCW	0	0	0	5	0
Participant 7	GentleWave	Necrotic/AAA	75	Female	Maxillary	PM	I	2	VB	30.04	BC	SC	0	25	25	25	25
Participant 8	GentleWave	AIP/Normal	39	Female	Mandibular	Molar	I	2	ES Scout	30.04	BC HiFlow	MCW	20	15	15	5	0
Participant 9	GentleWave	Necrotic/SAP	33	Female	Maxillary	Molar	I	2	VB	30.04	BC	SC	10	5	0	0	0
Participant 10	GentleWave	Necrotic/AAP	31	Male	Mandibular	Molar	I	2	VB	30.04	BC HiFlow	MCW	0	3	5	0	0
Participant 11	GentleWave	Necrotic/CAA	68	Male	Maxillary	Molar	I	1	VB	25.04	All plus	MCW	30	30	40	10	0
Participant 12	GentleWave	SIP/SAP	75	Female	Mandibular	Molar	I	2	VB	25.04	All plus	MCW	0	5	10	15	5
Participant 13	GentleWave	SIP/SAP	32	Female	Mandibular	PM	I	1	ES Scout	25.04	All plus	MCW	0	20	0	0	0
Participant 14	GentleWave	Necrotic/CAA	28	Male	Mandibular	Molar	I	2	Viper	20.06	All plus	MCW	0	0	0	0	0
Participant 15	GentleWave	PT/SAP	42	Male	Mandibular	Molar	R	2	VB	40.04	BC	MCW	0	15	10	10	20
Participant 16	GentleWave	Necrotic/SAP	46	Female	Mandibular	Molar	I	2	VB	25.04	All Plus	MCW	0	25	10	0	0
Participant 17	GentleWave	AIP/CAA	60	Male	Mandibular	Molar	I	2	ES Scout	20.04	All Plus	MCW	0	10	0	0	0
Participant 18	GentleWave	Necrotic/SAP	39	Male	Mandibular	Molar	I	2	ES Scout	25.04	All Plus	MCW	0	20	0	0	0
	GentleWave	4 participants Lost															

Table 5: Statistical Data Characteristics

Data characteristics

	GentleWave	Standard	All	p-value
n	18	18	36	
age	46.67 (±17.91)	56.00 (±13.75)	51.33 (±16.43)	0.0891
gender (=Female)	8 (44.44%)	6 (33.33%)	14 (38.89%)	0.7324
dx				0.7658
=AIP/CAA	1 (5.56%)	0 (0.00%)	1 (2.78%)	
=AIP/Normal	1 (5.56%)	1 (5.56%)	2 (5.56%)	
=Necrotic/AAA	1 (5.56%)	2 (11.11%)	3 (8.33%)	
=Necrotic/AAP	2 (11.11%)	1 (5.56%)	3 (8.33%)	
=Necrotic/CAA	3 (16.67%)	1 (5.56%)	4 (11.11%)	
=Necrotic/SAP	4 (22.22%)	6 (33.33%)	10 (27.78%)	
=Previously tx/AAP	1 (5.56%)	0 (0.00%)	1 (2.78%)	
=PT/AAP	1 (5.56%)	1 (5.56%)	2 (5.56%)	
=PT/SAP	1 (5.56%)	2 (11.11%)	3 (8.33%)	
=RP/SAP	1 (5.56%)	0 (0.00%)	1 (2.78%)	
=SIP/Normal	0 (0.00%)	2 (11.11%)	2 (5.56%)	
=SIP/SAP	2 (11.11%)	2 (11.11%)	4 (11.11%)	
max.man (=Mandibular)	14 (77.78%)	8 (44.44%)	22 (61.11%)	0.0874
molar.pre (=Molar)	14 (77.78%)	12 (66.67%)	26 (72.22%)	0.7098
treatment (=I)	15 (83.33%)	15 (83.33%)	30 (83.33%)	> 0.9999
appts	1.83 (±0.38)	1.56 (±0.51)	1.69 (±0.47)	0.0746
rotary.fs				0.5332
=ES Scout	6 (33.33%)	5 (27.78%)	11 (30.56%)	
=VB	11 (61.11%)	13 (72.22%)	24 (66.67%)	
=Vtaper	1 (5.56%)	0 (0.00%)	1 (2.78%)	
maf	27.54 (±4.92)	30.32 (±3.20)	28.93 (±4.33)	0.0541
sealer				0.2351
=AH Plus	8 (44.44%)	4 (22.22%)	12 (33.33%)	
=BC	6 (33.33%)	7 (38.89%)	13 (36.11%)	
=BC HiFlow	4 (22.22%)	3 (16.67%)	7 (19.44%)	
=Kerr	0 (0.00%)	3 (16.67%)	3 (8.33%)	
=Roths	0 (0.00%)	1 (5.56%)	1 (2.78%)	
obturation.tech (=MCW)	16 (88.89%)	14 (77.78%)	30 (83.33%)	0.6547

Table 6: Data Analysis – Linear mixed effects model

```
Linear mixed model fit by REML. t-tests use Satterthwaite's method
[lmerModLmerTest]
Formula: pain.rating ~ group + time.from.treat + age + (1 | id)
   Data: pop.lmer.df

REML criterion at convergence: 1139.6

Scaled residuals:
    Min      1Q  Median      3Q     Max
-1.7166 -0.5513 -0.1923  0.4311  4.2808

Random effects:
 Groups   Name        Variance Std.Dev.
 id       (Intercept) 128.8    11.35
 Residual             104.9    10.24
Number of obs: 144, groups:  id, 36

Fixed effects:
                 Estimate Std. Error        df t value Pr(>|t|)
(Intercept)       3.90811    6.95792  34.17345   0.562    0.578
groupStandard     6.83091    4.33403  33.00000   1.576    0.125
time.from.treat  -0.07701    0.01358 107.00000  -5.669 1.23e-07 ***
age               0.17288    0.13375  33.00000   1.293    0.205
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
            (Intr) grpStn tm.fr.
groupStndrd -0.027
tim.frm.trt -0.132  0.000
age         -0.897 -0.288  0.000
```

Appendix II

Figure 2: 0-100 NRS-41 pre-op pain assessment

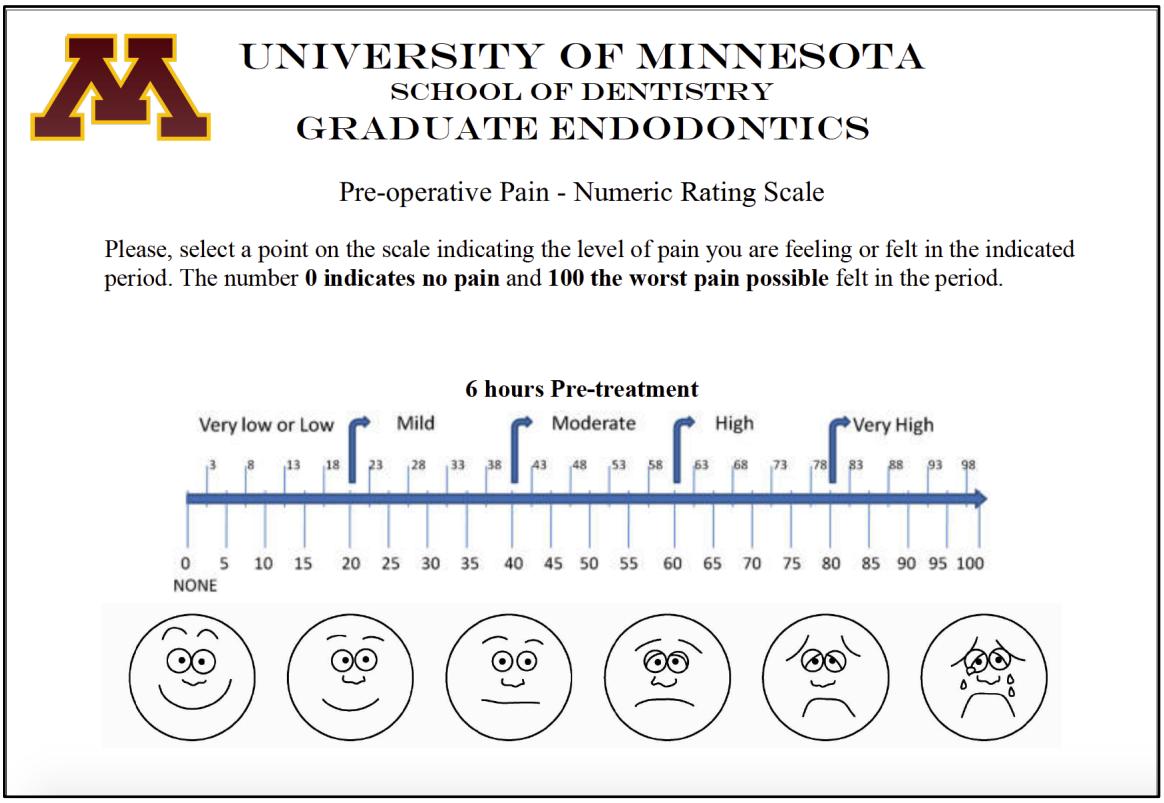


Figure 3: 0-100 NRS-41 post-op pain assessments